

Claims

1. A polypeptide comprising at least one binding peptide having an amino acid
5 sequence as indicated by the general formula (I) $X_1X_2X_3Y_1Y_2Y_3Y_4Y_1X_4X_5X_6$ or by the general formula (II) $X_7X_8X_9Y_1Y_2Y_3Y_4Y_1X_{10}Y_1X_{11}$, wherein

Y_1 is Cys

Y_2 is Arg

10 Y_3 is Gly

Y_4 is Asp

X_1 is Ala, Leu, Phe or Ser, in particular Ala or Leu;

X_2 is Arg, Leu, Phe, Pro, or Ser, in particular Arg or Ser;

X_3 is Ala, Gly, Leu, Ser, Tyr, or Val, in particular Gly, Leu, or Tyr;

15 X_4 is Gln, Phe, Ser, or Val, in particular, Phe or Val;

X_5 is Arg, Asp, Glu, or Gln, in particular Asp or Gln;

X_6 is Ala, Gln, Glu, Gly, Phe, or Val, in particular Ala, Gln or Gly;

X_7 is Glu, Phe, Pro, or Val, in particular Glu or Val;

X_8 is Ala or Cys, in particular Cys;

20 X_9 is Asp, Cys, Gln, or His, in particular Gln;

X_{10} is Leu, Phe, or Val, in particular Leu; and

X_{11} Gln, Phe, Pro, or Val, in particular Pro,

wherein X_1 , X_2 , X_3 , X_4 , X_5 , X_6 , X_7 , X_8 , X_9 , X_{10} , X_{11} , Y_1 , Y_2 , Y_3 , Y_4 are
25 independently of each other the D or L amino acid or the amino acid residue mimetic of the respectively indicated amino acid;

or said amino acid sequence, which lacks 1 or 2, preferably 1, amino acid(s) from the N-terminus or C-terminus or 1 amino acid from the N- and C-terminus.

- 30 2. The polypeptide of claim 1, wherein:

X_1 is Ala or Leu;

X_2 is Arg or Ser;

X₃ is Gly, Leu, or Tyr

X₄ is Phe or Val;

X₅ is Asp or Gln;

X₆ is Ala, Gln, or Gly;

5 X₇ is Glu or Val;

X₈ is Cys;

X₉ is Gln;

X₁₀ is Leu; and

X₁₁ is Pro.

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3. The polypeptide of claim 1, wherein the amino acid sequence is as shown in SEQ ID NOs 1 to 15.

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4. The polypeptide of one of claims 1 to 3 having a length of 100, preferably 20 and most preferably 12 amino acids.

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5. The polypeptide of one of claims 1 to 4, which comprises at least one amino acid sequence selected from the group consisting of a cytokine, a chemokine, a growth factor, an adhesion molecule, an antibody light and/or heavy chain, a single chain antibody, a toxin, an enzyme, a receptor ligand, a lytic peptide, a membrane insertion sequence and a fluorescent protein or fragments thereof.

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6. The polypeptide of one of claims 1 to 5, which is attached to at least one chemical moiety.

7. The polypeptide of claim 6, wherein the chemical moiety is selected from the group consisting of a spacer, a marker, a tag, a lipid, in particular a phospholipid, a drug, a capping group and a spacer attached to a second chemical moiety.

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8. The polypeptide of claim 7, wherein the spacer is selected from the group consisting of bifunctional polyethylenglycol and derivatives thereof, oligopeptides comprising between 1 to 40 natural or synthetic amino acids, 8-amino-3,6-dioxatanoic acid (doo), and (doo)_n, with n = 2-10.

9. The polypeptide of claim 7, wherein the marker is selected from the group consisting of an electron dense molecule, a paramagnetic molecule, a superparamagnetic molecule, a radioactive molecule, a non-radioactive isotope, and a fluorescent molecule.

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10. The polypeptide of claim 7, wherein the lipid is selected from the group consisting of glycerides, glycerophospholipides, glycerophosphinolipids, glycerophosphonolipids, sulfolipids, sphingolipids, phospholipids, isoprenolides, steroids, stearines, sterols, and carbohydrate containing lipids.

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11. The polypeptide of claim 10, wherein the phospholipid is selected from the group consisting of phosphatidylcholine (PC), phosphatidylserine (PS), and phosphatidylethanolamine (PE), in particular distearoylphosphatidyl (DSPE) or alpha-(dipalmitoyl)phosphatidyl (DPP).

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12. The polypeptide of claim 7, wherein the lipid is selected from the group consisting of N-caproylamine-PE, N-dodecanylamine-PE, phosphatidylthioethanol, N-[4-(p-maleimidomethyl)cyclohexane-carboxamide-PE (N-MCC-PE), N-[4-(p-maleimidophenyl)butyramide]-PE (N-MPB), N-[3-(2-pyridyldithio)propionate]-PE (N-PDP), N-succinyl-PE, N-glutaryl-PE, N-dodecanyl-PE, N-biotinyl-PE, N-biotinyl-cap-PE, phosphatidyl-(ethylene glycol), PE-polyethylene glycol (PEG)-carboxylic acid, PE-PEG-maleimide, PE-PEG-PDP, PE-PEG-amine, PE-PEG-biotin, PE-PEG-HNS, dipalmitoyl-glycerosuccinyl-lysine, alpha-methoxy-omega-(1,2-dioctadecenoyloxy glyceryl) (DO), alpha-methoxy-omega-(1,2-ditetradecenoyloxy glyceryl) (DT).

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13. The polypeptide of claim 7, wherein the second chemical moiety is selected from the group consisting of a drug, a marker, a tag, and a lipid.

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14. A polynucleotide encoding at least one polypeptide of claims 1 to 5.

15. The polynucleotide of claim 14 which is DNA or RNA.

16. A vector containing the polynucleotide of claim 14 or 15.

17. The vector of claim 10, wherein the polynucleotide is operatively linked to expression control sequences allowing expression in prokaryotic and/or eukaryotic host cells.
- 5 18. A host cell genetically engineered with the polynucleotide of claim 14 or 15 or the vector of claim 16 or 17.
- 10 19. A transgenic non-human animal containing a polynucleotide of claim 14 or 15, a vector of claim 16 or 17 and/or a host cell of claim 18.
20. An antibody specifically binding to the amino acid sequence within the polypeptides of claims 1 to 13.
- 15 21. A composition comprising at least one polypeptide of one of claims 1 to 13 and at least one further component selected from the group consisting of liposomes, virosomes, microspheres, niosomes, dendrimers, stabilizers, buffers, excipients and additives.
- 20 22. The composition of claim 21, wherein the polypeptide is integrated into or attached to the liposome, microspheres, niosomes, dendrimers, or virosome.
- 25 23. The composition of claim 21 or 22, wherein the liposome or virosome comprises lipids selected from the group consisting of glycerides, glycerophospholipides, glycerophosphinolipids, glycerophosphonolipids, sulfolipids, sphingolipids, phospholipids, isoprenolides, steroids, stearines, sterols, and carbohydrate containing lipids.
- 30 24. The composition of one of claims 21 to 23, wherein the liposome or virosome comprises cholesterol (CH) and sphingomyelin (SM).
25. The composition of claim 24, wherein CH and SM are present in relation to the total molar lipid composition of the liposome or virosome at a molar ratio of 40 to 60 mol% and 10 to 20 mol%, respectively.

26. The composition of claim 25, wherein CH and SM are present in relation to the total molar lipid composition of the liposome or virosome at a molar ratio of 48 to 52 mol% and 12 to 16 mol%, respectively.

27. The composition of one of claims 24 to 26 further comprising PE and/or PC.

28. The composition of claim 27, wherein PE and PC are present in relation to the total molar lipid composition of the liposome or virosome at a molar ratio of 5 to 25 mol% and 15 to 40 mol%, respectively.

29. The composition of claims 21 to 28 further comprising a drug selected from the group consisting of analgesics, antirheumatics, anthelmintics, antiallergics, antianemics, antiarrhythmics, antibiotics, angiogenesis inhibitors, antiinfectives, antidemenics (nootropics), antidiabetics, antidotes, antiemetics, antivertiginosics,, antiepileptics, antihemorrhagics, antihypertotics, antihypotonics, anticoagulants, antimycotics, antitussiv agents, antiviral agents, beta-receptor and calcium channel antagonists, broncholytic and antiastmatic agents, chemokines, cytokines, mitogens, cytostatics, cytotoxic agents and prodrugs thereof, dermatics, hypnotics and sedatives, immunosuppressants, immunostimulants, peptide or protein drugs, in particular hormones and physiological or pharmacological inhibitors of mitogens, chemokines, or cytokines or their respective prodrugs. Of course it is also envisioned that a liposome of the invention comprises more than one drug at once.

30. The compositions of claim 29, wherein the cytostatics and cytotoxic drugs are selected from the group consisting of alkylating substances, anti-metabolites, antibiotics, epothilones, nuclear receptor agonists and antagonists, anti-androgens, anti-estrogens, platinum compounds, hormones and antihormones, interferons and inhibitors of cell cycle-dependent protein kinases (CDKs), inhibitors of cyclooxygenases and/or lipoxygenases, biogenic fatty acids and fatty acid derivatives, including prostanoids and leukotrienes, inhibitors of protein kinases, inhibitors of protein phosphatases, inhibitors of lipid kinases, platinum coordination complexes, ethyleneimenes, methylmelamines, trazines, vinca alkaloids, pyrimidine

analog, purine analog, alkylsulfonates, folic acid analog, anthracendiones, substituted urea, methylhydrazin derivatives, in particular acediasulfone, aclarubicine, ambazone, aminoglutethimide, L-asparaginase, azathioprine, bleomycin, busulfan, calcium folinate, carboplatin, carpecitabine, carmustine, celecoxib, chlorambucil, cis-platin, cladribine, cyclophosphamide, cytarabine, dacarbazine, dactinomycin, dapsone, daunorubicin, dibrompropamide, diethylstilbestrol, docetaxel, doxorubicin, enedynes, epirubicin, epothilone B, epothilone D, estramucin phosphate, estrogen, ethinylestradiol, etoposide, flavopiridol, floxuridine, fludarabine, fluorouracil, fluoxymesterone, flutamide, fosfestrol, furazolidone, gemcitabine, gonadotropin releasing hormone analog, hexamethylmelamine, hydroxycarbamide, hydroxymethylnitrofurantoin, hydroxyprogesterone caproate, hydroxyurea, idarubicin, idoxuridine, ifosfamide, interferon α , irinotecan, leuprolide, lomustine, lurtotecan, mafenide sulfate, olamide, mechlorethamine, medroxyprogesterone acetate, megestrol acetate, melphalan, mepacrine, mercaptopurine, methotrexate, metronidazole, mitomycin C, mitopodizide, mitotane, mitoxantrone, mithramycin, nalidixic acid, nifuratel, nifuroxazide, nifuralazine, nifurtimox, nimustine, ninorazole, nitrofurantoin, nitrogen mustards, oleomucin, oxolinic acid, pentamidine, pentostatin, phenazopyridine, phthalylsulfathiazole, pipobroman, prednimustine, prednisone, preussin, procarbazine, pyrimethamine, raltitrexed, rapamycin, rofecoxib, rosiglitazone, salazosulfapyridine, scriflavinium chloride, semustine, streptozocine, sulfacarbamide, sulfacetamide, sulfachlopyridazine, sulfadiazine, sulfadiazole, sulfadimethoxine, sulfaethidole, sulfafurazole, sulfaguanidine, sulfaguanole, sulfamethizole, sulfamethoxazole, co-trimoxazole, sulfamethoxydiazine, sulfamethoxypyridazine, sulfamoxole, sulfanilamide, sulfaperin, sulfaphenazole, sulfathiazole, sulfisomidine, staurosporin, tamoxifen, taxol, teniposide, tertiposide, testolactone, testosterone propionate, thioguanine, thiotepa, tinidazole, topotecan, triaziquone, treosulfan, trimethoprim, trofosfamide, UCN-01, vinblastine, vincristine, vindesine, vinblastine, vinorelbine, and zorubicin, or their respective derivatives or analogs thereof.

31. Use of a polypeptide of one of claims 1 to 13 or of a composition of one of claims 21 to 30 for the production of a medicament for the therapy of proliferative diseases, immune diseases, in particular autoimmune diseases, infectious disease, a

vascular diseases, rheumatoid disease, in particular osteoarthritis and rheumatoid arthritis or diseases in which cells in or adjacent a disease site express $\alpha_v\beta_3$ and/or $\alpha_v\beta_5$ integrin, and inflammatory diseases.

- 5 32. The use of claim 31, wherein the proliferative disease is selected from the group consisting of carcinomas of the gastrointestinal or colorectal tract, liver, pancreas, kidney, bladder, prostate, endometrium, ovary, testes, melanoma, dysplastic oral mucosa, invasive oral cancers, small cell and non-small cell lung carcinomas, hormone-dependent breast cancers, independent breast cancers, transitional and
10 squamous cell cancers, neurological malignancies including neuroblastoma, gliomas, astrocytomas, osteosarcomas, soft tissue sarcomas, hemangioamas, endocrinological tumors, hematologic neoplasias including leukemias, lymphomas, and other myeloproliferative and lymphoproliferative diseases, carcinomas in situ, hyperplastic lesions, adenomas, fibromas, histiocytosis, chronic inflammatory
15 proliferative diseases, vascular proliferative diseases and virus-induced proliferative diseases.
33. The use of a polypeptide of claims 1 to 13 and/or a composition of claims 21 to 30 for the diagnosis of proliferative diseases, immune diseases, infectious diseases,
20 vascular diseases, rheumatoid diseases, inflammatory diseases, and diseases associated with an increase or decrease of the expression of $\alpha_v\beta_3$ and/or $\alpha_v\beta_5$ integrin.